Complete Summary

GUIDELINE TITLE

Prophylaxis of venous thromboembolism. A national clinical guideline.

BIBLIOGRAPHIC SOURCE(S)

Scottish Intercollegiate Guidelines Network (SIGN). Prophylaxis of venous thromboembolism. A national clinical guideline. Edinburgh (Scotland): Scottish Intercollegiate Guidelines Network (SIGN); 2002 Oct. 47 p. (SIGN publication; no. 62). [214 references]

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

Venous thromboembolism (deep vein thrombosis [DVT] with or without pulmonary embolism [PE])

GUIDELINE CATEGORY

Prevention
Risk Assessment

CLINICAL SPECIALTY

Anesthesiology
Cardiology
Emergency Medicine
Family Practice
Hematology
Internal Medicine

Neurological Surgery
Neurology
Obstetrics and Gynecology
Oncology
Orthopedic Surgery
Preventive Medicine
Surgery
Urology

INTENDED USERS

Advanced Practice Nurses
Nurses
Physician Assistants
Physicians

GUIDELINE OBJECTIVE(S)

To present evidence-based recommendations for the prophylaxis of venous thromboembolism in various populations

TARGET POPULATION

Patients potentially at risk for venous thromboembolism (VTE), including:

- Patients undergoing surgery (e.g. general, gynaecological, orthopaedic, trauma, urologic, neurologic, cardiothoracic, peripheral vascular, minimal access, other)
- Medical patients (e.g. patients with acute myocardial infarction, acute stroke, cancer; patients receiving antipsychotic drugs; other medical patients)
- Women who are pregnant, delivering, or in the puerperium
- Women on oral contraceptives and hormone replacement therapy
- Men and women undergoing long distance travel

INTERVENTIONS AND PRACTICES CONSIDERED

Risk Assessment/Prevention

1. Assessment of risk factors for venous thromboembolism (VTE), including personal risk factors, past history of venous thromboembolism, type of trauma, surgery (and anesthesia) or medical illness or condition
2. General prophylactic measures
    - Mobilisation and exercises
    - Hydration, haemodilution and venesection
3. Mechanical prophylactic methods
    - Graduated elastic compression stockings (GECS)
    - Intermittent pneumatic compression (IPC) devices
    - Mechanical foot pumps and foot impulse technology
4. Pharmacological prophylaxis
    - Antiplatelet agents (aspirin)

- Heparins (unfractionated and low molecular weight heparins) with monitoring of platelet count, bone density; reversal of heparin anticoagulation with protamine sulphate.
- Heparinoids (danaparoid)
- Hirudins (Desirudin, Lepirudin)
- Pentasaccharides (fondaparinux)
- Oral anticoagulants (Warfarin)
- Dextrans

5. Precautions prior to instituting spinal and epidural blocks
6. Counseling
    - Benefits and risks of prophylaxis
    - Risks of oral contraceptive and hormone replacement therapy as they relate to venous thromboembolism
    - Measures to reduce risk of thrombosis during long distance travel

MAJOR OUTCOMES CONSIDERED

- Risk and rate of asymptomatic deep vein thrombosis (DVT), symptomatic deep vein thrombosis, symptomatic venous thromboembolism (VTE), pulmonary embolism (PE), fatal pulmonary embolism, and total mortality
- Morbidity and mortality related to venous thromboembolism
- Safety, risks and adverse effects (especially bleeding) of pharmacological prophylaxis in various populations

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

The evidence base for this guideline was developed through a systematic review of the literature using an explicit search strategy developed by the Scottish Intercollegiate Guidelines Network (SIGN) Information Officer in collaboration with members of the guideline development group. Searches covered a number of key Internet sites as well as the CINAHL, Cochrane Library, Embase, Healthstar, and Medline databases. Systematic searches covered the period up until June 1998. Details of the main search strategy and supplementary searches carried out by a member of the guideline development group, are available on the SIGN website. The evidence base was updated during the development of the guideline.

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Levels of Evidence

1++
High quality meta-analyses, systematic reviews of randomised controlled trials (RCTs), or RCTs with a very low risk of bias

1+
Well-conducted meta-analyses, systematic reviews, or RCTs with a low risk of bias

1–
Meta-analyses, systematic reviews, or RCTs with a high risk of bias

2++
High quality systematic reviews of case control or cohort studies

High quality case control or cohort studies with a very low risk of confounding or bias and a high probability that the relationship is causal

2+
Well-conducted case control or cohort studies with a low risk of confounding or bias and a moderate probability that the relationship is causal

2–
Case control or cohort studies with a high risk of confounding or bias and a significant risk that the relationship is not causal

3
Non-analytic studies, e.g. case reports, case series

4
Expert opinion

METHODS USED TO ANALYZE THE EVIDENCE

Review of Published Meta-Analyses
Systematic Review with Evidence Tables

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

The Scottish Intercollegiate Guidelines Network (SIGN) carries out comprehensive systematic reviews of the literature using customized search strategies applied to a number of electronic databases and the Internet. This is often an iterative process whereby the guideline development group will carry out a search for existing guidelines and systematic reviews in the first instance and, after the results of this search have been evaluated, the questions driving the search may be redefined and focused before proceeding to identify lower levels of evidence.

Once papers have been selected as potential sources of evidence, the methodology used in each study is assessed to ensure its validity. SIGN has

developed checklists to aid guideline developers to critically evaluate the methodology of different types of study design. The result of this assessment will affect the level of evidence allocated to the paper, which in turn will influence the grade of recommendation it supports.

Additional details can be found in the companion document titled "SIGN 50: A Guideline Developers' Handbook." (Edinburgh [UK]: Scottish Intercollegiate Guidelines Network. [SIGN publication; no. 50], available from the SIGN Web site.)

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

The process for synthesizing the evidence base to form graded guideline recommendations is illustrated in the companion document titled "SIGN 50: A Guideline Developer's Handbook." (Edinburgh [UK]: Scottish Intercollegiate Guidelines Network. [SIGN publication; no. 50], available from the SIGN website.

Evidence tables should be compiled, summarizing all the validated studies identified from the systematic literature review relating to each key question. These evidence tables form an important part of the guideline development record and ensure that the basis of the guideline development group's recommendations is transparent.

In order to address how the guideline developer was able to arrive at their recommendations given the evidence they had to base them on, SIGN has introduced the concept of considered judgement.

Under the heading of considered judgement, guideline development groups are expected to summarise their view of the total body of evidence covered by each evidence table. This summary view is expected to cover the following aspects:

- Quantity, quality, and consistency of evidence
- Generalisability of study findings
- Applicability to the target population of the guideline
- Clinical impact (i.e., the extent of the impact on the target patient population, and the resources need to treat them.)

Guideline development groups are provided with a pro forma in which to record the main points from their considered judgement. Once they have considered these issues, the group are asked to summarise their view of the evidence and assign a level of evidence to it, before going on to derive a graded recommendation.

The assignment of a level of evidence should involve all those on a particular guideline development group or subgroup involved with reviewing the evidence in relation to each specific question. The allocation of the associated grade of

recommendation should involve participation of all members of the guideline development group. Where the guideline development group is unable to agree a unanimous recommendation, the difference of opinion should be formally recorded and the reason for dissent noted.

The recommendation grading system is intended to place greater weight on the quality of the evidence supporting each recommendation, and to emphasise that the body of evidence should be considered as a whole, and not rely on a single study to support each recommendation. It is also intended to allow more weight to be given to recommendations supported by good quality observational studies where randomised controlled trials (RCTs) are not available for practical or ethical reasons. Through the considered judgement process guideline developers are also able to downgrade a recommendation where they think the evidence is not generalisable, not directly applicable to the target population, or for other reasons is perceived as being weaker than a simple evaluation of the methodology would suggest.

On occasion, there is an important practical point that the guideline developer may wish to emphasise but for which there is not, nor is their likely to be, any research evidence. This will typically be where some aspect of treatment is regarded as such sound clinical practice that nobody is likely to question it. These are marked in the guideline as "good practice points." It must be emphasized that these are not an alternative to evidence-based recommendations, and should only be used where there is no alternative means of highlighting the issue.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

The grade of recommendation relates to the strength of the evidence on which the recommendation is based. It does not reflect the clinical importance of the recommendation.

Grade A: At least one meta-analysis, systematic review of randomized controlled trials (RCTs), or randomized controlled trial rated as 1++ and directly applicable to the target population; or

A body of evidence consisting principally of studies rated as 1+, directly applicable to the target population, and demonstrating overall consistency of results

Grade B: A body of evidence including studies rated as 2++, directly applicable to the target population, and demonstrating overall consistency of results; or

Extrapolated evidence from studies rated as 1++ or 1+

Grade C: A body of evidence including studies rated as 2+, directly applicable to the target population and demonstrating overall consistency of results; or

Extrapolated evidence from studies rate as 2++

Grade D: Evidence level 3 or 4; or

Extrapolated evidence from studies rated as 2+

Good Practice Points: Recommended best practice based on the clinical experience of the guideline development group.

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

Comparison with Guidelines from Other Groups
External Peer Review
Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Internal and External Peer Review

A national open meeting is the main consultative phase of the Scottish Intercollegiate Guidelines Network (SIGN) guideline development, at which the guideline development group presents their draft recommendations for the first time. The national open meeting for this guideline was held on 13th December 1999. The draft guideline was also available on the SIGN website for a limited period at this stage to allow those unable to attend the meeting to contribute to the development of the guideline.

The guideline is reviewed in draft form by a panel of independent expert referees, who are asked to comment primarily on the comprehensiveness and accuracy of interpretation of the evidence base supporting the recommendations in the guideline.

As a final quality control check, the guideline is reviewed by an Editorial Group comprising the relevant specialty representatives on SIGN Council to ensure that the peer reviewers comments have been addressed adequately and that any risk of bias in the guideline development process as a whole has been minimised.

Comparison of Guideline with Other Groups

Recommendations regarding aspirin as effective prophylaxis from the following guideline was discussed: A North American guideline (American College of Chest Physicians, 2001).

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Note from the Scottish Intercollegiate Guidelines Network (SIGN) and National Guideline Clearinghouse (NGC): In addition to these evidence-based recommendations, the guideline development group also identifies points of best clinical practice in the original guideline document.

The strength of recommendation grading (A-D) and level of evidence (I++-4) are defined at the end of the "Major Recommendations" field.

Risk Factors for Venous Thromboembolism (VTE)

D: All patients admitted to hospital for major trauma (e.g. fracture causing immobilisation), major surgery (e.g. duration over 30 mins), or acute medical illness (e.g. likely to require bed rest for three days or more) should be individually assessed for risk of VTE.

D: Assessment of individual risk should include:

- personal risk factors for VTE (see Table 1 in the original guideline document)
- past history of VTE (hospitalisation increases risk of recurrent VTE)
- type of trauma, surgery (and anaesthesia) or medical illness

D: Local guidelines should be developed and updated for specific patient groups.

D: Within local guidelines, individual prophylaxis should be chosen according to the balance of efficacy and risks (especially bleeding), and the patient's preferences.

D: Routine screening for thrombophilias prior to risk situations such as prescription of oral contraceptives or hormone replacement therapy, pregnancy, or elective major surgery is not recommended.

Methods of Prophylaxis

General Measures

C: Early mobilisation and leg exercises should be encouraged in patients recently immobilised.

D: Adequate hydration should be ensured in immobilised patients.

Mechanical Methods

Graduated Elastic Compression Stockings (GECS)

A: GECS are effective in prophylaxis of asymptomatic deep vein thrombosis (DVT) and symptomatic pulmonary embolism (PE) in surgical patients.

GECS Plus Pharmacological Prophylaxis or Intermittent Pneumatic Compression

A: GECS may be combined with pharmacological prophylaxis or intermittent pneumatic compression (IPC) in surgical patients, to increase efficacy in reducing the incidence of DVT.

Intermittent Pneumatic Compression

A: IPC devices are effective in prophylaxis of asymptomatic DVT in surgical patients.

A: IPC plus low dose heparin reduces the risk of symptomatic PE in cardiac surgery patients.

Mechanical Foot Pumps and Foot Impulse Technology

A: Mechanical foot pumps are effective in prophylaxis of asymptomatic DVT in orthopaedic surgery patients.

Antiplatelet Agents (Aspirin)

A: Aspirin 150 mg/day started preoperatively and continued for 35 days is effective prophylaxis of asymptomatic and symptomatic VTE in surgical patients. Aspirin also reduces cardiovascular events in acute MI and acute ischaemic stroke.

Unfractionated and Low Molecular Weight Heparins (UFH and LMWHs)

Efficacy and Safety of UFH and LMWHs in Medical Patients

A: Subcutaneous low dose heparin (UFH or LMWH) is effective in prophylaxis of asymptomatic and symptomatic VTE in surgical and medical patients.

Monitoring Platelet Count

B: In order to detect heparin associated thrombocytopenia, a baseline platelet count should be obtained and platelet count monitored in all patients receiving heparins for five days or more.

A: Heparin should be stopped if thrombocytopenia develops, or if the platelet count drops by 50% or more. Possible alternative initial antithrombotics include lepirudin.

B: Warfarin is a suitable alternative antithrombotic to heparin following heparin associated thrombocytopenia, once the platelet count has recovered to >100 x 10^9/L.

Oral Anticoagulants

D: In patients receiving long term oral anticoagulant therapy who are immobilised by illness, trauma or surgery, continuation of oral anticoagulants (target INR [international normalized ratio] 2.0-2.5) may be appropriate prophylaxis.

D: The combination of UFH or LMWH with mechanical prophylaxis may be an effective alternative to continuing oral anticoagulants in selected surgical patients.

General and Gynaecological Surgery

Heparins

Low Molecular Weight Heparins

A: The preferred methods of prophylaxis (because they reduce mortality as well as fatal PE) in patients undergoing major general or gynaecological surgery who are at significant risk of VTE are:

subcutaneous low-dose UFH (5,000 IU, 8-12 hourly)

or

subcutaneous LMWH (dose as per manufacturer's instructions)

Mechanical Methods

Graduated Elastic Compression Stockings

A: In patients undergoing major general or gynaecological surgery GECS can be substituted for UFH or LMWH when these agents are contraindicated.

A: GECS can be combined with UFH or LMWH in patients undergoing general or gynaecological surgery who are at high risk due to the presence of multiple risk factors.

Intermittent Pneumatic Compression

A: In patients undergoing major general or gynaecological surgery, IPC followed by above-knee GECS can be substituted for UFH or LMWH when these agents are contraindicated.

Antiplatelet Drugs (Aspirin)

A: Aspirin (150 mg/day orally, rectally or by nasogastric tube) is an alternative to UFH or LMWH when these agents are contraindicated in patients undergoing major general or gynaecological surgery who are at significant risk of VTE.

Dextrans

A: Intravenous dextran 40 or 70 is a possible alternative prophylaxis of VTE in high risk patients undergoing major general or gynaecological surgery.

Orthopaedic Surgery and Trauma

Total Hip or Knee Replacement

Mechanical Prophylaxis

A: Patients undergoing total hip or knee replacement (or other elective major orthopaedic surgery) can be considered for mechanical prophylaxis (GECS ± IPC or foot pumps).

Antiplatelet drugs (aspirin)

A: Patients undergoing total hip or knee replacement (or other elective major orthopaedic surgery) can be considered for aspirin (150 mg orally, started before surgery and continued for 35 days).

Heparins

A: Patients undergoing total hip or knee replacement (or other elective major orthopaedic surgery) can be considered for UFH or LMWH.

A: The duration of UFH or LMWH prophylaxis should be 7-15 days after lower limb arthroplasty, extended to 4-5 weeks in very high-risk patients.

Oral Anticoagulants

A: Patients undergoing major orthopaedic surgery (e.g. total hip or knee replacement) can be considered for warfarin (target INR 2.0-3.0), e.g. those already receiving warfarin.

Summary

A: Patients undergoing total knee or hip replacement (or other elective major orthopaedic surgery) should receive thromboprophylaxis: mechanical (GECS ± IPC, foot pumps), pharmacological (aspirin or heparin or warfarin), or both.

Hip Fracture Surgery

C: Early surgery (within 24 hours) is recommended where possible to reduce the risk of DVT and fatal PE after hip fracture.

Mechanical Prophylaxis

A: Mechanical prophylaxis (IPC or foot pumps) should be considered to reduce the risk of asymptomatic DVT after hip fracture. There is no evidence for the efficacy of GECS in hip fracture patients.

Antiplatelet Drugs (Aspirin)

A: All patients with hip fracture should receive aspirin (150mg orally, started on admission and continued for 35 days) unless contraindicated.

Heparins

A: Heparin should be reserved for selected patients at high risk of VTE after hip fracture due to:

- multiple risk factors (see "Risk Factors for Thromboembolism" above)
- contraindications to routine mechanical prophylaxis and/or aspirin

Trauma

A: In patients with spinal cord injury, major lower limb fractures or multiple trauma, LMWH prophylaxis can be considered, unless contraindicated (e.g. by risk of intracranial bleeding).

A: In patients with contraindications to LMWHs, mechanical prophylaxis can be considered (e.g. IPC or foot pump).

C: In patients in whom LMWH is contraindicated and mechanical prophylaxis is not feasible (e.g. patients in plaster casts), aspirin (150mg/day), started on admission and continued for 35 days can be considered.

Other Types of Surgery

Urological Surgery

Major or Open Urological Procedures

A: The preferred method of prophylaxis in patients undergoing major or open urological procedures who are at significant risk of VTE (age over 40 or other risk factors) is: subcutaneous low-dose UFH (5,000 IU, 8-12 hourly) or subcutaneous LMWH (dose as per manufacturer's instructions).

B: In patients in whom UFH or LMWH are contraindicated, mechanical prophylaxis (GECS ± IPC) can be considered.

Transurethral Resection of the Prostate (TURP)

C: In patients undergoing transurethral resection of the prostate who are at increased risk of VTE due to multiple risk factors, antithrombotic prophylaxis with UFH, LMWH, or GECS ± IPC should be considered.

Neurosurgery

A: Neurosurgical patients should receive antithrombotic prophylaxis using mechanical methods (GECS ± IPC).

A: LMWH can also be considered in neurosurgical patients, but there is an increased risk of haemorrhage.

Cardiothoracic Surgery

B: In patients undergoing major cardiothoracic surgery who are at significant risk of VTE, subcutaneous low-dose UFH or LMWH are recommended. Mechanical prophylaxis (GECS ± IPC) is an alternative.

A: In patients undergoing cardiac surgery, the addition of IPC to heparin prophylaxis should be considered.

A: Aspirin should be discontinued prior to elective cardiac bypass surgery because of the risks of bleeding, and resumed (75-300 mg/day) via nasogastric tube six hours following bypass grafting and continued long term in patients with symptomatic arterial disease.

Peripheral Vascular Surgery

Major Vascular Surgery

C: In patients with critical limb ischaemia or who are undergoing major peripheral vascular surgery (including amputation), subcutaneous low-dose UFH or LMWH is recommended.

A: Aspirin (75-300 mg/day) should be given or resumed (via nasogastric tube) starting six hours following bypass grafting and continued long term.

Varicose Vein Surgery

C: In patients undergoing varicose vein surgery who have no additional risk factors for VTE, postoperative GECS are recommended.

C: In the presence of additional risk factors (e.g. previous DVT or PE, prolonged surgery or immobility) the addition of subcutaneous UFH or LMWH is recommended.

Minimal Access Surgery

C: In patients undergoing minimal access surgery who have additional risk factors, or who are undergoing major prolonged procedures, subcutaneous UFH or LMWH is recommended.

C: In lower-risk patients mechanical prophylaxis (GECS ± IPC) is recommended.

Spinal and Epidural Blocks

Efficacy in Prophylaxis of VTE in Surgical Patients

A: Spinal or epidural anaesthesia may be preferred to general anaesthesia where appropriate and feasible.

Risk of Vertebral Canal Haematoma When Combined with Pharmacological Prophylaxis of VTE

Recommendations

D: When instituting spinal/epidural block prior to elective surgery, epidural catheter removal or diagnostic lumbar puncture, the following precautions should be taken:

- Aspirin: proceed normally, but remember interactions

- UFH: proceed normally but exercise caution
    - or administer 4-6 hours before block
    - or delay first dose until after block performed or until after surgery
- LMWH: administer 10-12 hours before block
- Warfarin: if INR <1.5 proceed normally
    - if INR ≥1.5 delay surgery or consider alternative anaesthetic or anaesthetic technique if surgery is urgent.

Medical Patients

Acute Myocardial Infarction (MI)

Antiplatelet Drugs (Aspirin) and Thrombolytic Therapy

A: It is strongly recommended that all patients with clinically suspected evolving acute MI who are not already receiving aspirin should be given aspirin (150-300 mg).

A: It is strongly recommended that all patients with clinically suspected evolving acute MI should be considered for thrombolytic therapy.

Anticoagulants

A: Heparin should not be used routinely in addition to aspirin in acute MI, but reserved for patients at increased thromboembolic risk (and for certain patients undergoing thrombolysis).

A: Patients with acute, established MI at increased risk of systemic or pulmonary thromboembolism due to:

- large anterior Q-wave infarction
- severe left ventricular dysfunction
- congestive heart failure
- history of systemic or pulmonary embolism or thrombophilia
- echocardiographic evidence of mural thrombus
- persistent atrial fibrillation
- prolonged immobilisation
- marked obesity

should be considered for anticoagulation with full-dose heparin (target activated partial thromboplastin time [APTT] ratio 2.0, range 1.5-2.5) followed (if indicated by continuing risk) with warfarin (target INR 2.5, range 2.0-3.0) for up to three months, depending upon the physician's estimate of the risk:benefit ratio in the individual patient.

A: In other patients with acute MI, and in patients as defined above in whom the bleeding risks of full-dose anticoagulation are judged to outweigh the benefits, prophylaxis of VTE with low-dose subcutaneous heparin (7,500 IU 12-hourly) for seven days or until ambulant, should be considered.

Mechanical Prophylaxis

A: Compression stockings may be considered in patients with acute MI who are at increased risk of VTE, especially when heparin prophylaxis is contraindicated.

Acute Stroke

Mechanical Prophylaxis

C: Selected use of graduated compression stockings may be justified for some high risk patients.

D: Compression stockings are preferred for patients with haemorrhagic stroke.

Antiplatelet Drugs (Aspirin)

A: Early treatment with aspirin (initially 150-300 mg/day) is recommended in acute ischaemic stroke, starting as soon as intracranial haemorrhage is excluded by computed tomography (CT) or magnetic resonance (MR) brain scanning, for risk reduction in death and cardiovascular events, including DVT and PE.

Heparins

A: UFH (e.g. 5,000 IU subcutaneously twice a day) or a LMWH may be considered in patients with ischaemic stroke who are judged to be at higher than average risk of VTE (e.g. history of previous VTE, known thrombophilia or active cancer) and lower than average risk of haemorrhagic complications.

Other Medical Patients

Heparins

A: In general medical patients who are immobilised in hospital due to acute illness, especially those with heart failure, respiratory failure, infections, diabetic coma, inflammatory bowel disease, nephrotic syndrome, or in intensive care, prophylaxis of VTE with low dose UFH or LMWH should be considered. LMWH carries a lower risk of bleeding.

Mechanical Methods

C: In general medical patients at significant risk of VTE in whom heparin prophylaxis is contraindicated, GECS may be considered.

Cancer Patients

A: Minidose warfarin (1 mg/day, no INR monitoring) is recommended for prophylaxis of thrombosis in cancer patients with central venous catheters.

A: Low-dose warfarin (target INR 1.6, range 1.3-1.9) is recommended for prophylaxis of thrombosis during chemotherapy in stage IV breast cancer.

Pregnancy and the Puerperium

B: Warfarin and other coumarins should be avoided if possible during pregnancy, at least between six and 12 weeks gestation and after 36 weeks' gestation.

B: LMWH is preferred to UFH in pregnancy, as there is more safety data.

D: All pregnant women should be regularly assessed for VTE risk factors.

Antenatal Thrombosis Risk Assessment

D: All pregnant women with a personal history of VTE, or a family history of VTE in first or second degree relatives, should be offered screening for thrombophilias.

Previous VTE and No Identifiable Thrombophilias

C: In all women with VTE events during previous pregnancy or combined oral contraceptive (COC) use, antenatal thromboprophylaxis should be started as early as possible in pregnancy.

C: In all women with previous idiopathic VTE, antenatal prophylaxis should be started as early as possible in pregnancy.

B: Women in whom a previous VTE occurred in association with other temporary risk factors, which are no longer present (e.g. surgery or trauma), and who have no identifiable thrombophilia or current risk factors other than pregnancy, do not routinely require antenatal LMWH prophylaxis, but should be considered for GECS.

C: Where antenatal thromboprophylaxis is appropriate, it should be:

- subcutaneous LMWH (e.g. 40mg enoxaparin daily or 5,000 IU dalteparin daily). The platelet count should be checked before and one week after the introduction of LMWH
- at low body weight, e.g. <50kg, lower doses of LMWH may be required (e.g.20mg enoxaparin daily or 2500 IU dalteparin daily)
- in obese patients, (e.g. body mass index [BMI] >30 in early pregnancy), higher doses of LMWH may be required
- GECS may be combined with LMWH. Clinical surveillance for evidence of VTE should also be considered

C: All women with a past history of VTE should receive thromboprophylaxis postpartum (see "Delivery and the Puerperium" below).

Long Term Anticoagulants or Known Heritable Thrombophilia

High Risk of Clinical VTE (>1:40)

C: In pregnant women at high risk of VTE, prophylaxis should be subcutaneous LMWH, (e.g. enoxaparin 0.5-1mg/kg 12 hourly or dalteparin 50-100 IU/kg 12 hourly), based on the early pregnancy weight. The platelet count should be checked before and one week after the introduction of LMWH.

Moderately Increased Risk of Clinical VTE (1:40-1:200)

C: In pregnant women at moderately increased risk of VTE, prophylaxis can be given as LMWH (e.g. enoxaparin 40mg daily or dalteparin 5,000 IU daily). The platelet count should be checked before and one week after the introduction of LMWH.

Antiphospholipid Syndrome

A: Women with antiphospholipid syndrome and recurrent miscarriage should receive thromboprophylaxis from the diagnosis of pregnancy with LMWH (e.g. enoxaparin 40 mg daily or dalteparin 5,000 IU daily) and low dose aspirin (75 mg/day).

C: Women with antiphospholipid syndrome who have already had a thrombotic event should receive low dose aspirin (75 mg/day) and LMWH (e.g. enoxaparin 40mg daily or dalteparin 5,000 IU daily) from the diagnosis of pregnancy.

C: Other women with antiphospholipid syndrome should receive low dose aspirin (75 mg/day) antenatally to reduce the risk of pregnancy complications, and postpartum heparin prophylaxis (see "Delivery and the Puerperium" below).

Delivery and the Puerperium

Management of Delivery

C:

- In pregnant women who have requested epidural anaesthesia during labour, stop the administration of LMWH when labour starts.
- LMWH can be administered or readministered three hours after atraumatic epidural or spinal anaesthesia, or removal of an epidural catheter.

Management of the Puerperium

C: Postpartum thromboprophylaxis is recommended in women with:

- previous VTE (or family history)
- known thrombophilias
- other thrombotic risk factors

C: Postpartum, the first dose of subcutaneous LMWH (enoxaparin 40mg daily or dalteparin 5,000 U daily) should be given 3-6 hours after delivery.

C: Postpartum anticoagulation should be continued for a minimum of six weeks in patients with previous VTE or thrombophilias. In other patients, prophylaxis should continue until discharge from hospital; review need for prophylaxis if hospital stay continues beyond five days.

C: Where the patient does not wish to continue self-injecting, LMWH can be replaced by warfarin starting on the first or second postpartum day. The LMWH can be withdrawn when the INR has been within the target range (usually 2.0 - 3.0) for two consecutive days.

C: There is no contraindication to breast feeding when the mother is being treated with LMWH, warfarin or other coumarins.

C: GECS can be added to LMWH in high risk patients and should be used where LMWH is contraindicated.

Heparin Contraindications in Pregnancy and Puerperium

Haemorrhage

C: Where anticoagulants are contraindicated, GECS should be worn for at least six weeks following delivery. This may be combined with low dose aspirin (75 mg/day).

Oral Contraceptives and Hormone Replacement Therapy

Hormone Replacement Therapy (HRT) and Raloxifene

C: Women starting combined oral contraceptives (COC), higher dose progestogens, oral HRT or raloxifene should be advised of the small absolute increased risk of VTE. They should have a personal and family history taken of VTE and of additional risk factors for thromboembolic disease (e.g. obesity: see Table 1 in the original guideline document).

C: A personal history of VTE is a contraindication to the use of COC and oral HRT.

C: A history of VTE in a first degree family member is a relative contraindication to use of COC, higher dose progestogens, oral HRT or raloxifene, irrespective of the results of thrombophilia screening.

C: In current (or recent) COC, higher dose progestogen, HRT or raloxifene users who are undergoing surgery, it is recommended that medical practitioners:

- discuss the balance of risks and benefits with the patient when considering stopping these hormones prior to elective surgery
- arrange adequate alternative contraception if COC is to be discontinued
- consider specific antithrombotic prophylaxis according to overall risk factors (see Table 1 in the original guideline document)
- give VTE prophylaxis routinely in emergency surgery

Long Distance Travel

D: To minimise the risk of thrombosis when travelling long distances (e.g. over four hours), especially by air, all travellers should be advised to:

- ensure good hydration
- restrict alcohol and coffee intake
- regularly carry out simple leg exercises and take occasional walks during travel

D: In patients at high risk of thrombosis (e.g. previous DVT or PE; known thrombophilia; recent major trauma, surgery or immobilising medical illness, pregnancy), the following prophylactic methods should be considered:

- GECS
- a single dose of aspirin (150 mg) before travel (± GECS)
- a single injection of a LMWH before travel in prophylactic dose (See "Methods of Prophylaxis" above) (± GECS)
- patients already receiving warfarin should continue to take it (± GECS). INR should be checked one week before long distance travel and the dose adjusted to within the target therapeutic range

D: The risks of bleeding should be considered (e.g. increased risk of major bleed with aspirin or heparins, which is difficult to treat on a long haul flight), and the balance of risks and benefits should be discussed with the individual patient.

Definitions:

Levels of Evidence

1++
High quality meta-analyses, systematic reviews of randomised controlled trials (RCTs), or RCTs with a very low risk of bias

1+
Well-conducted meta-analyses, systematic reviews, or RCTs with a low risk of bias

1–
Meta-analyses, systematic reviews, or RCTs with a high risk of bias

2++
High quality systematic reviews of case control or cohort studies

High quality case control or cohort studies with a very low risk of confounding or bias and a high probability that the relationship is causal

2+
Well-conducted case control or cohort studies with a low risk of confounding or bias and a moderate probability that the relationship is causal

2–
Case control or cohort studies with a high risk of confounding or bias and a significant risk that the relationship is not causal

3
Non-analytic studies, e.g. case reports, case series

4
Expert opinion

Grades of Recommendation

Note: The grade of recommendation relates to the strength of the evidence on which the recommendation is based. It does not reflect the clinical importance of the recommendation.

A
At least one meta-analysis, systematic review of randomised controlled trials (RCTs), or RCT rated as 1++ and directly applicable to the target population; or

A body of evidence consisting principally of studies rated as 1+, directly applicable to the target population, and demonstrating overall consistency of results.

B
A body of evidence including studies rated as 2++, directly applicable to the target population, and demonstrating overall consistency of results; or

Extrapolated evidence from studies rated as 1++ or 1+.

C
A body of evidence including studies rated as 2+, directly applicable to the target population and demonstrating overall consistency of results; or

Extrapolated evidence from studies rated as 2++.

D
Evidence level 3 or 4; or

Extrapolated evidence from studies rated as 2+.

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The specific type of supporting evidence is explicitly identified in each section of the guideline.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Appropriate Prophylaxis of Venous Thromboembolism Might:

- Decrease the risk and rate of asymptomatic deep vein thrombosis (DVT), symptomatic deep vein thrombosis, symptomatic venous thromboembolism (VTE), pulmonary embolism (PE), fatal pulmonary embolism, and total mortality

- Decrease the morbidity and mortality related to venous thromboembolism
- Help manage the risk of adverse effects of pharmacologic prophylaxis, especially major bleeding

POTENTIAL HARMS

Side Effects of Drugs

The primary risk of antiplatelet agents (aspirin), heparins, and warfarin is bleeding.

CONTRAINDICATIONS

CONTRAINDICATIONS

Aspirin and Heparins

Contraindications for aspirin and heparins in prophylaxis of venous thromboembolism (VTE)

- Uncorrected bleeding disorders, e.g. haemophilias, oral anticoagulants, platelet count $<70x10^9$/L
- Bleeding or potentially bleeding lesions (oesophageal varices, active peptic ulcer, gastrointestinal or intracranial bleed within 3 months, intracranial aneurysm or angioma)
- Allergy
- Heparin associated thrombocytopenia or thrombosis (heparin)

Cautions for aspirin and heparins in prophylaxis of venous thromboembolism

- Asthma (aspirin)
- Severe liver impairment, alcoholism
- Severe kidney impairment
- Major trauma or surgery to brain, eye or spinal cord
- Spinal or epidural block
- Anaemia (hemoglobin <10 g/dl)

Anticoagulants

Contraindications and cautions for oral anticoagulants (Warfarin)

- Bleeding disorders
- Bleeding or potentially bleeding lesions
- Spinal or epidural anaesthesia
- Pregnancy, due to fetal toxicity

Graduated Elastic Compression Stockings (GECS)

Contraindications

- Massive leg oedema
- Pulmonary oedema (e.g. heart failure)
- Severe peripheral arterial disease
- Severe peripheral neuropathy
- Major leg deformity
- Dermatitis

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

All Recommendations Apply Only in the Absence of Contraindications

This guideline is not intended to be construed or to serve as a standard of medical care. Standards of care are determined on the basis of all clinical data available for an individual case and are subject to change as scientific knowledge and technology advance and patterns of care evolve. The ultimate judgement regarding a particular clinical procedure or treatment plan must be made in light of the clinical data presented by the patient and the diagnostic and treatment options available.

However, it is advised that significant departures from the national guideline or any local guidelines derived from it should be fully documented in the patient's case notes at the time the relevant decision is taken.

Literature Review

Because of the timing of this review, this guideline was not developed using current methodology and does not meet current standards in terms of documentation of the evidence base and considered judgement process.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

Local Implementation

Implementation of national clinical guidelines is the responsibility of each National Health Service (NHS) Trust and is an essential part of clinical governance. It is acknowledged that every Trust cannot implement every guideline immediately on publication, but mechanisms should be in place to ensure that the care provided is reviewed against the guideline recommendations and the reasons for any differences assessed and, where appropriate, addressed. These discussions should involve both clinical staff and management. Local arrangements may then be made to implement the national guideline in individual hospitals, units and practices, and to monitor compliance. This may be done by a variety of means including patient-specific reminders, continuing education and training, and clinical audit.

It is recommended that hospitals in Scotland should:

- ensure that local guidelines are in place for relevant surgical, medical and family planning patients
- update existing local guidelines in accordance with the revised national guideline
- perform clinical audit at appropriate intervals

Key points for audit, information on resource implications, and key messages for patients admitted to the hospital are identified in the original guideline document.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Staying Healthy

IOM DOMAIN

Effectiveness
Patient-centeredness
Safety

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Scottish Intercollegiate Guidelines Network (SIGN). Prophylaxis of venous thromboembolism. A national clinical guideline. Edinburgh (Scotland): Scottish Intercollegiate Guidelines Network (SIGN); 2002 Oct. 47 p. (SIGN publication; no. 62). [214 references]

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2002 Oct

GUIDELINE DEVELOPER(S)

Scottish Intercollegiate Guidelines Network - National Government Agency [Non-U.S.]

SOURCE(S) OF FUNDING

Scottish Executive Health Department

GUIDELINE COMMITTEE

Not stated

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Guideline Development Group: Professor Gordon Lowe (Chairman); Mr Michael Aitchison; Mrs Moira Balmer; Professor Jill Belch; Mr Ivan Brenkel; Professor Ian Greer; Mr Robin Harbour; Dr John Irving; Ms Brenda Jackson; Mr Nizam Mamode; Dr Safia Qureshi; Mr Lech Rymaszewski; Professor Peter Sandercock; Ms Lorna Thomson; Dr Isobel Walker; Professor Tony Wildsmith

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

All members of the Scottish Intercollegiate Guidelines Network (SIGN) guideline development groups are required to complete a declaration of interests, both personal and non-personal. A personal interest involves payment to the individual concerned, e.g., consultancies or other fee-paid work commissioned by or shareholdings in the pharmaceutical industry; a non-personal interest involves payment which benefits any group, unit or department for which the individual is responsible, e.g., endowed fellowships or other pharmaceutical industry support. SIGN guideline group members should be able to act as independently of external commercial influences as possible, therefore, individuals who declare considerable personal interests may be asked to withdraw from the group. Details of the declarations of interest of any guideline development group member(s) are available from the SIGN executive.

GUIDELINE STATUS

This is the current release of the guideline.

Any amendments to the guideline in the interim period will be noted on the Scottish Intercollegiate Guidelines Network (SIGN) Web site.

GUIDELINE AVAILABILITY

Electronic copies: Available from the Scottish Intercollegiate Guidelines Network (SIGN) Web site:

- HTML Format
- Portable Document Format (PDF)

AVAILABILITY OF COMPANION DOCUMENTS

The following is available:

- Quick reference guide: Prophylaxis of venous thromboembolism, Scottish Intercollegiate Guidelines Network, 2002. 2 p. Available in Portable Document Format (PDF) from the Scottish Intercollegiate Guidelines Network (SIGN) Web site.
- SIGN 50: a guideline developers' handbook. Edinburgh (UK): Scottish Intercollegiate Guidelines Network. (SIGN publication; no. 50). Available from the SIGN Web site.

- Appraising the quality of clinical guidelines. The SIGN guide to the AGREE (Appraisal of Guidelines Research & Evaluation) guideline appraisal instrument. Edinburgh (UK): Scottish Intercollegiate Guidelines Network, 2001. Available from the SIGN Web site.
- Additional supporting documentation is available from the SIGN Web site.

PATIENT RESOURCES

The following is available:

- Key messages for patients admitted to hospital. In: Prophylaxis of venous thromboembolism. A national clinical guideline. Edinburgh (Scotland): Scottish Intercollegiate Guidelines Network (SIGN); 2002 Oct. 47 p. (SIGN publication; no. 62).

Electronic copies: Available from the Scottish Intercollegiate Guidelines Network (SIGN) Web site:

- HTML Format
- Portable Document Format (PDF)

Please note: This patient information is intended to provide health professionals with information to share with their patients to help them better understand their health and their diagnosed disorders. By providing access to this patient information, it is not the intention of NGC to provide specific medical advice for particular patients. Rather we urge patients and their representatives to review this material and then to consult with a licensed health professional for evaluation of treatment options suitable for them as well as for diagnosis and answers to their personal medical questions. This patient information has been derived and prepared from a guideline for health care professionals included on NGC by the authors or publishers of that original guideline. The patient information is not reviewed by NGC to establish whether or not it accurately reflects the original guideline's content.

NGC STATUS

This NGC summary was completed by ECRI on February 21, 2003. The information was verified by the guideline developer on March 12, 2003.

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